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Ultrasound

MEDICAL APPLICATIONS, BIOLOGICAL EFFECTS, AND HAZARD POTENTIAL

The pressure vessel was built to the specifications of the American Society of Mechanical Engineers Boilers and Pressure Vessel Code to withstand 60 atm and was large enough to accomodate a stereotaxic head holder for the cat, the insonation head and a 3-axis transpositioning system to permit measurement of T_{IB}, local and systemic temperature monitoring subsystem, acoustic emission monitoring transducer, systemic (core) temperature control system to maintain the desired core temperature, various feed-throughs for electrical connections and hydraulic lines, and incorporated safety devices to protect against overpressurization. Tests were conducted on methyl-methacrylate phantoms[47] to ascertain that the output of the insonation system and the characteristics of the coupling medium and temperature and acoustic emission measurement systems were not affected by cyclical pressure changes.

Measurements of acoustic emission were made for insonation at different intensities for each of several burst durations between 0.1 and 10.0 sec. for single or multiple bursts. Intensity or burst duration was increased or decreased progressively in consecutive insonations, or was varied in a random manner. The influence of ambient pressure and the base temperature of the animal under pressures of 1 and 42 atm on acoustic emission, as well as on the size of resultant lesions, was studied. In parallel experiments the T_{IB} and the peak temperatures in the tissue at the center of the insonation beam were measured with an implanted 50 μ thermocouple. At least 6, generally 10 and frequently up to 25 replicates were obtained for each data point and subjected to statistical analyses.

All tissues insonated in vivo and samples of tissues insonated in vitro were examined histologically for morphological alterations. The presence and nature of these were then correlated with that of acoustic emission measured previously. Modelling and analytical studies were also undertaken to understand the physical mechanisms by which insonation induced cavitation may damage mammalian tissues. These are not included in this paper; some of the early work was reported previously[41].

Acoustic Emissions

Representative recordings of the typical swept frequency spectra and the time course of acoustic emissions from air-saturated water, degassed deionized water, bovine plasma, and from cat brain in vivo during a burst of insonation are presented in Figs. 9 and 10. In the frequency domain the emission from air-saturated water (Fig. 9A) is characterized by a strong signal at the fundamental and the half-harmonic and relatively weaker signals at the second, third and higher harmonics. In all of the media the amplitude of the signal at the fundamental was found to be invariably proportional to the square root of the insonation power indicating that it was the result of the direct coupling between the insonation and receiver transducers, through the medium or its boundaries (glass, air or skull), and was not associated with cavitation activity. In the time-domain (Fig. 9B), the half-harmonic emission from air-saturated water is seen as sharp "spikes" or a burst of spikes, occurring only during insonation, but randomly with respect to its beginning or end. Though the half-harmonic emissions were thus random, both in occurrence and amplitude, it was obvious from an analysis of hundreds of records of integrated power output that their time-averaged energy content was statistically stable and constant at any particular insonation intensity. Below a certain threshold insonation intensity there was no emission at any anharmonic frequency,

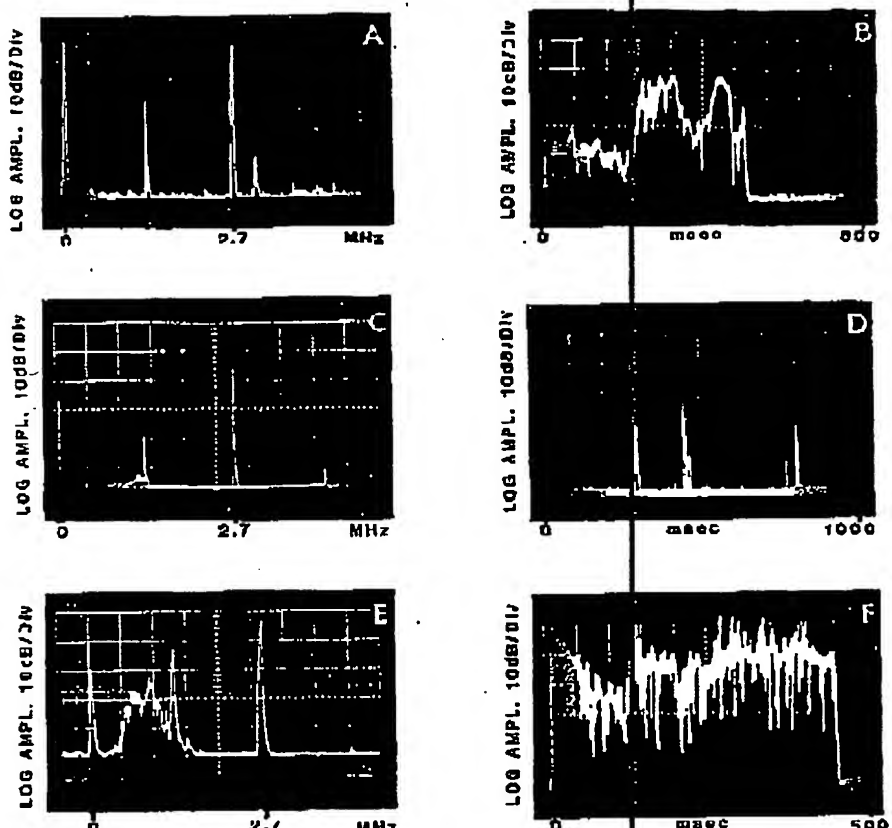

Fig. 9. Representative records of acoustic emission from air-saturated water (A,B), degassed deionized water (C,D), and bovine blood plasma (E,F) in frequency (Left) and time (Right) domains. The vertical axis shows the logarithmic amplitude (10 dB/div.) of the acoustic emission with the average base line due to instrument noise at -100dBm ($=10^{-13}$W). The scales for the horizontal axes are as shown on each record.

that is, at frequencies other than the harmonics of the half-harmonic or the fundamental frequency. If, however, the peak focal insonation intensity exceeded a threshold value (which was dependent on the medium, as well as on the insonation frequency), then in addition to the harmonic and half-harmonic emissions and their harmonics, erratic wideband emissions, with rise and fall times of the order of a microsecond, were observed. The frequency spectrum of these wide-band emissions encompassed the frequency bandwidth of the receiver, with an essentially flat power distribution. It was therefore concluded that the magnitude of the anharmonic emission at 4.6 MHz ± 150 kHz could be used for quantification of the wide-band emission, and the associated bubble collapse type of cavitation (unstable cavitation). Acoustic emission from degassed, deionized water (Figs. 9C,D) was found to be similar to that from air-saturated water, but of significantly lower magnitude (approx.-40 dB) at each insonation intensity, whereas that from bovine blood plasma (Figs. 9E,F) was consistently of greater magnitude (approx. +3dB) and of wider bandwith centered at a frequency below the

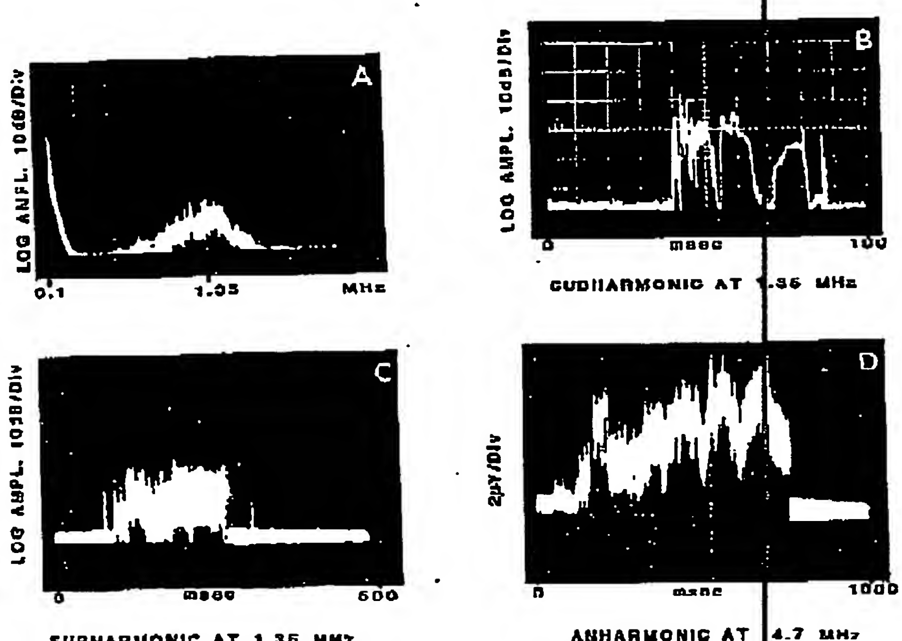

Fig. 10. Representative records of acoustic emission from the brain of the cat _in vivo_, in frequency (A) and time domains (B,C,D). Records B, C : Subharmonic emission: D: Anharmonic emission.

half-harmonic spike. The bandwidth of the comparable emission from the calf liver *in vitro* and from the brain of the cat *in vivo* (Fig. 10A) was found to be even wider and was centered around the half-harmonic frequency. This progressive increase in the bandwidth of acoustic emission from water to plasma to brain, on theoretical considerations, was believed to be due to the progressively higher viscous damping in the three media. This was confirmed in a study of acoustic emission from a series of progressively more viscous solutions of increasing concentrations of glycerol in water. Based on these considerations, the term 'subharmonic' is used hereafter in this article to include the half-harmonic 'spike' when present.

Intensity and Frequency Dependence of Acoustic Emission

Subharmonic and ultraharmonic emissions were measured for a burst 0.5 sec in duration, at insonation frequencies of 2.7 and 1.8 MHz, varying the peak focal intensity in the medium, in steps from 100 mW.cm^{-2} to 3,100 W.cm^{-2}. The averaged values for 10 or more replicates under each insonation condition showed a monotonic increase in subharmonic

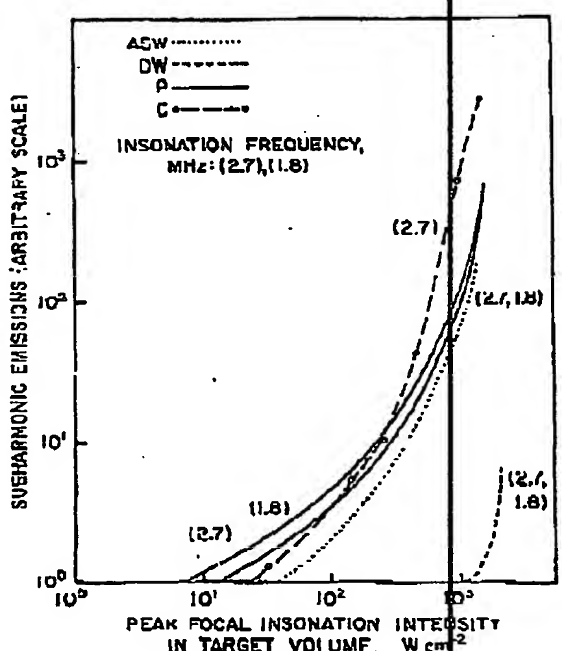

Fig. 11. Intensity and frequency dependence of subharmonic emission from air-saturated water (ASW), degassed deionized water (DW) and bovine blood plasma (P) and the brain of the cat *in vivo* (C) for 0.5 sec burst at insonation frequencies of 1.8 and 2.7 MHz. Values for peak focal intensity are corrected for attenuation in each medium.

emission with intensity from 150 mW.cm^{-2} to 1,500 W.cm^{-2} (Fig. 11), although there was no distinct threshold intensity for the occurrence of the emission. Above the intensity of 1,500 W.cm^{-2}, there was a remarkably sharp increase, of many orders of magnitude, in the subharmonic emission (Fig. 12). The magnitude of the emission from plasma and from the brain of the cat in vivo was only slightly greater than that from air-saturated water, the emission from which was 2 to 3 orders of magnitude greater than that from degassed, deionized water. Comparison of data at insonation frequencies of 2.7 and 1.8 MHz (Fig. 11) showed no significant differences in the emission from water, but slightly higher levels of emission was evident from plasma at the lower insonation frequency.

No anharmonic emission was ever observed at peak focal intensities of 1,000 W.cm^{-2} in air saturated water, calf liver in vitro or in brain of the cat in vivo even with burst durations of up to 10 sec. It occurred only sporadically at intensity levels between 1,000 W.cm^{-2} and 1,500 W.cm^{-2}. But above 1,500 W.cm^{-2} there was an abrupt and marked increase in anharmonic emission (Figs. 10D,13), as well as in subharmonic emission (Fig. 12) and both types of emission were detected at each insonation at intensities above 3000 W.cm^{-2}. Compared to that in air saturated water, the 'threshold' for the onset of anharmonic emission from the tissues is lower, and at intensities above the threshold, the energy content of the emission from the tissues is found to be approximately two orders of magnitude higher than that from air-saturated water. This lower threshold and higher acoustic emission from biological tissues implies not only the presence of a larger number of cavitation sites and nuclei, but possibly also the higher probability of retaining the oscillating bubble(s) within the insonation focus for longer periods

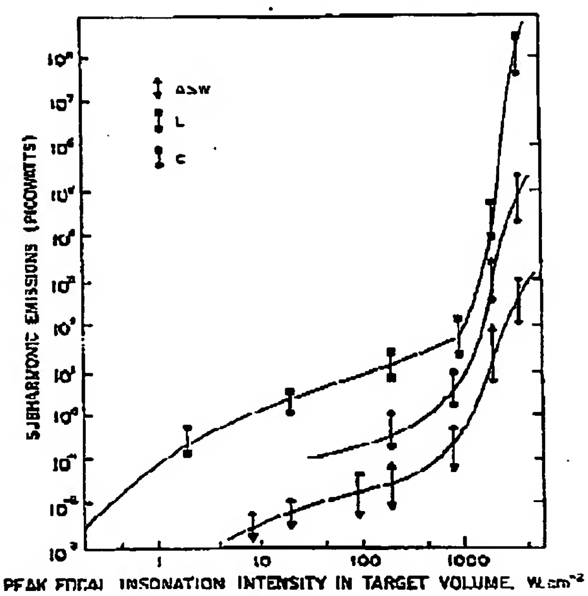

Fig. 12. Intensity dependence of subharmonic emission from air-saturated water (ASW), calf liver in vitro (L), and brain of the cat in vivo (C), for a 0.5 sec burst at insonation frequency of 2.7 MHz. The vertical lines indicate the spread in data.

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